

draws a like conclusion concerning a somewhat similar case of combination of the two diseases in the ileum, lacking, however, the extreme connective tissue and muscular hyperplasia noted here.

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EMBRYONAL RENAL ADENOSARCOMA.

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AMONG the tumors of the kidney we find very peculiarly interesting types having a very peculiar histogenesis. We may mention in this connection those neoplasms arising from inclusions of displaced suprarenal tissue, known now more generally as hypernephroma. There is a type of mixed tumors of the kidney which has been attracting attention for a number of years, the true character of which, however, has been fully recognized only quite recently. These mixed renal tumors occur very early in life, frequently during the first years. They are not very common, but comparatively rare. They generally first attract attention not by any urinary symptoms, particularly not by hæmaturia, but by the increasing size of the abdomen. They grow very rapidly, speedily lead to general malignant cachexia, and destroy the life of the victim either with or without the formation of metastases. These tumors always develop inside of the kidney; the kidney tissue proper, however, does not take part in the proliferating neoplastic processes, but becomes compressed by the new growth and atrophic. Uriniferous tubules and their lining epithelia disappear in consequence of pressure atrophy. What is left of the kidney sometimes sits on the tumor like a flat cap. In other cases neoplasms of this kind proliferate toward the pelvis of the kidney, projecting into it in the form of polypoid masses. These malignant renal tumors of early childhood are so heterologous in their histology that they have been described as carcinoma, sarcoma, endothelioma, rhabdomyoma, and under a variety of compound names.

We are indebted to Birch-Hirschfeld¹ for having first successfully cleared up the confusion which reigned as to these new growths. This author, in his paper on "Renal Tumors," points out that the common histological feature of these neoplasms is the fact that they present a

mixture of epithelial-adenomatous and connective tissue elements, and that all of these are proliferating in a most extensive embryonal manner. In the description of these neoplasms Birch-Hirschfeld states that sometimes the character of an adenoma predominates, while the connective tissue elements are less prominent; at other times the opposite prevails. These variable conditions are found not only in different tumors, but in different parts of the same neoplasm. These tumors very frequently contain striated muscle fibres, which in some of the reported cases were present in so large an amount that the new growths were designated as rhabdomyoma or rhabdomyosarcoma.

These tumors do not tend to form early metastases, but, on the contrary, lead to the latter only after the growth has become so very large that it has by pressure broken through the capsule. The neighboring lymphatics are not affected even if the adenomatous type predominates. Speaking about the classification of these peculiar renal tumors, Birch-Hirschfeld says: "We can only classify as pure sarcomata such neoplasms as arise from a proliferation of archiblastic elements without any active participation of epithelial tissues. It appears, *à priori*, possible that there occur in the kidney sarcomata very closely related to the adenosarcomatous mixed tumors. These pure sarcomata presumably would arise from embryonal inclusions equivalent to those archiblastic elements, giving origin to the adenosarcomata, only that the former do not contain any glandular (epithelial) tissue. Tumors of this type might be considered as simple embryonal renal sarcomata."

Birch-Hirschfeld believes that the embryonal renal adenosarcomata take their origin from remnants of the Wolffian body, and gives Eberth credit for having been the first one to suggest this possibility with reference to embryonal tumors of the kidney containing epithelial elements. Eberth tried to explain the presence of striated muscle fibres upon the ground that the connective tissue of the Wolffian body was rich in embryonal muscle cells.

This point is, however, not well taken. The embryonal tissue Eberth refers to gives rise to non-striated, but not to striated muscle fibres.

Birch-Hirschfeld, in advocating the view that the mixed renal tumors take their origin from remnants of the Wolffian body, says that such an origin would explain the intimate relation between the tumor and the kidney and pelvis on the one hand, and the lack of a true blending between kidney substance and tumor tissue on the other.

Since Birch-Hirschfeld published his article upon these embryonal renal tumors there has appeared another very important contribution upon this subject by Wilms,⁷ and while we cannot indorse all of this author's views on the histogenesis and histology of these neoplasms, we gladly recognize his as a most excellent and exhaustive study of the subject.

Wilms, in reviewing Birch-Hirschfeld's idea as to the histogenesis of these tumors, says: "Birch-Hirschfeld traces the origin of these tumors back to embryonic inclusions derived from the Wolffian body. However, I think that this attempt at explanation only accounts for the presence of epithelial elements, but the question remains unanswered whence arise the other heterologous elements such as striated muscle fibres, cartilage," etc.

On this point Wilms very appropriately says that the Wolffian body does not give rise to any striated muscle fibres, and that embryonic inclusions derived solely from the Wolffian body cannot be considered sufficient to account for all of the constituents of the peculiar mixed renal tumors of childhood.

If one reads Wilms' comments, one first gains the impression that he repudiates entirely any attempt to make remnants of the Wolffian body responsible for these tumors, and that he looks for the histogenesis of them in embryonic inclusions from the myotomes. It appears settled that the myotomes are those embryonal structures which give rise to the entire system of striated muscles. Cohnheim, as Wilms himself states, had already given it as his opinion that the rhabdomyoma of the kidney arise from embryonic inclusions of myotome tissue. If one, however, discards the Wolffian body entirely and looks to the myotomes alone, one finds indeed the source of the striated muscle fibres and the cartilage, but not the origin of the epithelial structures which these tumors contain. To surmount this difficulty, Wilms, toward the close of his monograph, gives it as his view that the mixed renal tumors under discussion arise from inclusion of the very earliest embryonic development, namely, from an undifferentiated mesodermal tissue which later on, in normal embryonic development, gives rise to the Wolffian body and to the myotome. To support this view Wilms is compelled to assume certain metaplastic processes in the development of these tumors. But these metaplastic processes have not been observed elsewhere, nor can Wilms furnish the least proof that they do occur in the mixed renal tumors. Wilms assumes that the inclusion of the very early undifferentiated embryonic tissue, which later on would give rise to the Wolffian body and the myotomes, forms, when it develops the tumor, irregular masses of round cells. That the latter are differentiated into epithelial cells, nay, more, that these, first present in irregular masses, differentiate themselves later into epithelial glandular tissue. Wilms' own words with reference to this process are as follows (*loc. cit.*, p. 62): "The epithelial glands (*Drüesenschläuche*) in the tumor, according to our view, are not of primary origin, but they arise from certain cells of an embryonal tissue still undergoing differentiation. They arise from cells in which, in consequence of our inadequate means, we cannot see future epithelial cells, but which appear first as small round cells in an embryonic tissue."

This view of Wilms appears utterly untenable if one compares it with what is known about normal processes of embryonic differentiation. Where do we find in normal embryonic metaplasia or differentiation of the human embryo any process in which small embryonal round cells later on become epithelia, first aggregated in irregular masses, and these then giving rise to regular tubular glands?

Wilms, in contesting Birch-Hirschfeld's view (which we indorse), that the glandular formations are the primary structures, and that the irregular cell masses are derived from the glands, says: "Against the view that the regular gland spaces are primarily and the cell masses secondarily formed speak several factors. First, the most complete epithelial structures are mostly found in the middle of the tumor. While in the younger parts of the tumor, where we have the youngest proliferation, we only find rudimentary ("angedeutete") glands and large irregular cell masses. In other words, where we have a recent growth we have either only irregular masses of round cells or an attempt (andeutung) at gland formation. . . . In one of our renal tumor cases we found in a detached focus in the suprarenal gland not a single regular gland space, but only cell masses which show the beginning of a glandular arrangement," etc.

These arguments, particularly the statement that the tubular arrangement of epithelial elements is most distinct in the oldest and not in the youngest parts of the tumor, do not at all speak in favor of Wilms' views. Quite the contrary, all the facts cited clearly indicate that the irregular cell masses are the product of a proliferation of epithelial cells which primarily had a tubular arrangement. It is one of the best known and now most uniformly recognized facts of neoplastic proliferation, that the metaplasia of the tumor cells becomes the greater the more removed the latter are in time and space from their original progenitors. Let us look at any malignant epithelial neoplasm. We find that the newly-formed cells first deviate comparatively little from the mother cells from which they sprang. The further we get away from the original starting-point of the tumor the greater, as a rule, is the deviation from the original cell type. This state of affairs becomes generally best marked when we compare metastases with the original tumor. These points have been dwelt upon in a very exhaustive manner by Hanseman.³ It is very clear that Wilms' detached focus of a renal tumor in a suprarenal capsule, which he cites as a proof of his theory, was a metastasis, and as such showed a large degree of anaplasia and metaplasia of the original tumor cells. While it is one of the most common occurrences to find in tumors a regressive metaplasia, which, as one of us⁴ has pointed out elsewhere, may have the character of a truly atavistic metaplasia, it would be an unheard-of condition in malignant tumors to find such a progressive metaplasia as Wilms claims these renal tumors repre-

sent. There seems to be no reason for the adoption of Wilms' hypothesis. The very facts, as he describes them, speak against it.

To give our own views as to the histogenesis of these tumors, it is necessary to enter very briefly into a discussion of the development of the myotomes ("ursegmente") and of the Wolffian body ("urniere"). These structures are developed from the early mesoderm which is first differentiated into the myotome and the lateral plate. Between these structures there is formed a thin bridge known as the nephrotome ("mittelplatte"). In the latter the transverse excretory tubules of the Wolffian body, emptying later on into the Wolffian duct, are formed. While these tubules develop the nephrotome becomes entirely cut off from the myotomes. This is in short the normal course of events.

With reference to the embryonal renal adenosarcomata of childhood, we assume that they owe their origin to an inclusion which is formed in the following manner: The nephrotome is not cut off at the normal site, but in such a manner that a part of the myotome is severed from the main mass and remains in connection with the nephrotome. The separation may take place, so that only a part of the myotome proper is cut off, or a part of the sclerotome may likewise be taken along. If the former is the case, we have the matrix for striated muscle fibres only; if the latter occurs, we have also the matrix for cartilage. If now we assume that a part of the nephrotome (Wolffian body) to which tissues of the myotome proper, or the latter and the sclerotome have become adherent by an abnormal process of embryonic separation, becomes included in the permanent kidney, we have a matrix containing all those embryonic elements which occur in the mixed renal tumors, namely, striated muscle fibres, cartilage, other connective tissue elements, and epithelial glandular structures. The latter, of course, are derived from the excretory tubules of the nephrotome.

This explanation appears to us the most feasible one; it will account for the character of these peculiar renal neoplasms without compelling us to take refuge, as Wilms does, in metaplastic processes unheard of in tumor formation.

In examining these tumors it is also necessary to consider Brosius'⁴ views, that the adenomatous tissue in those neoplasms is not truly epithelial, but of a lymphatic endothelial character. If this were the case, one could without difficulty understand an origin from inclusions of the myotomes alone, since the latter contain lymphatic tissue. A close examination of the glandular spaces and cell masses, however, shows that we are dealing beyond doubt with true epithelial elements. The sections show distinctly that the epithelial nests are sharply defined. They do not gradually fuse into the surrounding connective tissue as in an endothelioma. Wilms, who cites the view of Brosius as to the endo-

thelial nature of the cell nests, only does so to at once discard it, as do other authors who have studied the subject.

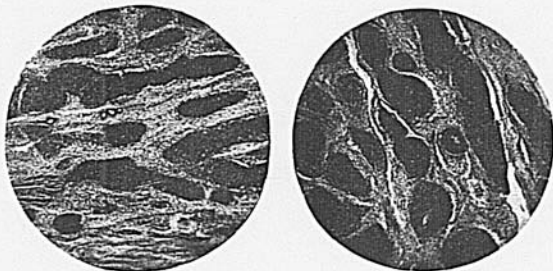
The following is a short abstract of the history of the case which we want to report in this paper :

August 2, 1898. The child, operated upon by one of us (Lewis) on this date, was a female white child, sixteen months old, weighing twenty-one and one-half pounds before the operation. The tumor weighed five and one-half pounds. The circumference of the abdomen was twenty-three inches. The child, which had to all appearances been normal when born, developed well and was in good health until May, 1898. Then there was noticed some gastro-intestinal disturbance; however, no diarrhoea. The child then vomited a black substance, and the parents thought that the child had swallowed a piece of the nurse's dress. Dr. Lewis saw the child in June; it was then suffering from a slight bronchitis, which disappeared after three days. About this time there was also noticed a marked swelling of the abdomen. This swelling increased rapidly, and the general health of the child began to fail. A diagnosis of tumor of the abdomen and later sarcoma of the kidney was made. A urinary analysis failed to show albumin or casts. On July 31, 1898, Dr. Walter S. Christopher saw the child in consultation. He concurred in the diagnosis of sarcoma of the kidney. The operation was performed August 2, 1898, by Dr. Lewis, assisted by Drs. Weller, Van Hook, and Henry Norton, and in the presence of Drs. Almon Brooks and N. H. Henderson. The abdomen was opened by a transverse incision over the most prominent part. The tumor had formed very numerous adhesions to the intestines. These adhesions were separated without rupturing the gut anywhere. The pedicle of the tumor was then ligated and the new growth removed. The abdominal incision was closed; an opening of about one inch was left, through which the gauze dressing protruded. When the operation was completed at 3 p.m. the child appeared to be in good condition; the temperature was below 100°, the pulse good. A number of hours after the operation the child took some nourishment, which was retained. The gauze was removed twenty-six hours after the operation; no pus or blood. Thirty hours after the operation the temperature rose to 103°, and within an hour collapse and death followed. The exitus occurred thirty-one hours after the operation. On the following day Dr. Lewis made a partial autopsy. The intestines were found moderately distended with gas, no rupture, no blood, no pus. No metastases were found in the abdomen.

The tumor after removal was more or less globular in general outlines, but somewhat flattened above and below and at the lateral surfaces. The largest diameter extends from side to side and measures 18 to 19 cm.; the largest circumference is 58 to 59 cm. A fairly strong, shining, transparent capsule, nowhere broken through, but intact, invests the neoplasm. The lower surface of the new growth presents a crater-like depression 3 to 4 cm. deep. An incision made at this place shows that we have here located what is left of the compressed remnant of the kidney. The surface of the tumor is coarsely nodular, in consequence of the fact that the neoplasm is composed of a number of roundish nodular masses which vary in size from a hazelnut to a fist. All these masses are surrounded by the common capsule. The larger masses, as can be seen on the incised surface, are again composed of smaller

nodules, each one surrounded by fibrous connective tissue septa. The interior of the tumor generally shows a tissue of a fibro-sarcomatous character, but there are also places which convey the impression of carcinomatous tissue. These two kinds of tissues are not intermixed in a heterologous manner, but are, on the contrary, quite separate and distinct. The difference in the macroscopic appearance of different parts

FIG. 1.



Sections through adenomatous parts of the tumor showing alveolar epithelial nests and tubular glands. $\times 50$.

FIG. 2.

FIG. 3.

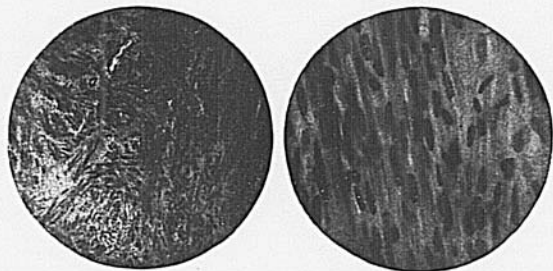


FIG. 2.—Section showing interlacing bundles of striated embryonal muscle fibres. $\times 50$.

FIG. 3.—The same; oil-immersion magnification.

of the tumor is explained by the microscopic examination. The parts looking like a carcinoma are made up of epithelial nests and tubular structures, the parts having a fibro-sarcomatous appearance are composed of connective tissue elements.

The compressed remnant of the kidney substance proper forms a conical or pyramidal mass, the apex of which projects into the crater-like depression of the under surface. The base of the cone has a

diameter of 6 cm. ; the distance from base to apex measures 3 cm. One is able to distinguish in what is left of the kidney the cortical and the medullary substances. Kidney substance and tumor are very distinct from each other. It appears that the latter has nowhere actually broken into the kidney substance.

The microscopical examination shows that the tumor is composed of two different kinds of tissue, epithelial structures and of connective tissue elements. These two types of tissue are distributed throughout the tumor in such a manner that we find in some places a pure picture of an epithelial neoplasm, while other places present the type of an embryonal connective tissue neoplasm. There is nowhere found in the examination of many sections either an intimate blending or a chaotic mixture of the two different types of tissue. They remain, on the contrary, discrete, and each one strictly preserves its own type. In this manner there is created a strong impression that the two kinds of tissue had originated quite separately.

The epithelial elements present themselves in the form of alveolar nests surrounded by connective tissue. Very frequently one sees either more or less in the middle, or situated quite eccentrically in the cell nests, tubular gland spaces. The epithelia lining the latter have very typical vesicular nuclei, possessing a moderate amount of finely granular chromatin, which is distributed in a peripheral manner to the inside of the nuclear membrane. The cell body is cuboidal, the protoplasm of moderate amount. The lumen of the glandular spaces so formed has approximately the size of a larger uriniferous tubule. One also finds glandular lumina of greatly enlarged size. The interior of such large gland spaces is filled with desquamated cells in a state of hydropic swelling. Gland spaces are, however, not only found in the interior of solid cell nests, but outside of them. Such tubular glands are lined by epithelial cells of the character described, and these single rows of epithelia are directly surrounded by connective tissue. The majority of the cells forming the solid nests deviate to a certain degree from the type of the epithelia which line the gland spaces. The former possess more chromatin than the latter, and the increased amount of chromatin fills the nucleus more densely. The latter deviates quite markedly from the character of a typically vesicular nucleus, and looks more like a granular nucleus. The cell protoplasm of the cells of the nests is not cuboidal, but round. *If one compares these cells with those lining the tubules which empty into the Wolffian ducts of human embryos about 12 to 14 mm. long, one is struck by the great similarity which exists between them.* The epithelial nests show neither a fibrillar nor any other stroma, but the alveoli contain exclusively the cells described. These cells also never show transitional forms leading over to the surrounding connective tissue. Such transitional forms are, as is well-known, always found in endotheliomata. But a picture which might create the suspicion that we are possibly dealing in our case with an endothelioma is not found.

The connective tissue areas of the tumor generally give the picture of a pure rhabdomyoma. A small amount of the striated muscle fibres of the tumor very much approaches the type of adult normal striated muscle. The fibres are cylindrical, the longitudinal, as well as the transverse striæ, are very distinct. The oval nuclei are situated on the sarcoplasm directly under the sarcolemma. In such places, where we also find other signs of degenerative processes, the muscle fibres just

described show fragmentation, and they are broken up into the component disks. In general, however, the type which approaches very much normal muscle fibres is only rarely found, and the embryonal, not fully differentiated type, predominates to a large extent. The major part of the tumor is composed of fibres containing several large oval or rod-like nuclei. Whether these cells have a sarcolemma or not cannot be made out. The nuclei are not on top of the protoplasm, but, as can be distinctly seen in transverse sections, inside of the sarcoplasm. The striation is distinct, but very fine. This second class of cells found in the rhabdomyomatous parts of the tumor shows the characters of striated muscle cells as found in the early embryo of mammals.

The muscle cells of this type unite to form bundles, and these interlace each other in an apparently irregular manner. The tissue so formed contains numerous small bloodvessels. The capsule of the tumor consists of densely packed fibres and slender fusiform cells. Remnants of kidney tissue could not be found in the tumor itself, neither was cartilage encountered.

In concluding the microscopical description of the tumor tissue we want to again state expressly that the epithelial as well as the connective tissue elements show an exquisite embryonal type, which is rarely found so very well pronounced in tumors. Sections from the kidney tissue proper show well-marked degenerative changes in the epithelia, particularly in those lining the convoluted tubules. The cells are swollen, indistinct in outlines, the protoplasm is cloudy, and the nucleus either faintly stained or entirely absent. The lumen of the tubules lined with degenerating epithelia frequently contains granular matter, occasionally hyaline matter. Other tubules show a free lumen and normal epithelia. In places completely collapsed tubules are seen. The limbs of Henle show the least changes, and many appear normal. The most prominent changes are found in the glomeruli, the majority of which is atrophic. The change, however, does not consist in a true degeneration, such as, for instance, a hyaline degeneration, but in a true atrophy. The capsule of the atrophic glomeruli is likewise very small and surrounds the latter so closely that there is only left a small lumen. The small atrophic glomeruli are so densely studded with nuclei that it is difficult to distinguish them individually even in thin sections and with high power. The glomeruli appearing normal as to size, likewise show an increased number of nuclei. It appears that there has taken place in consequence of the insult of pressure a proliferative reaction of the vascular endothelium of the glomerular capillaries. Aside from this evident proliferation of vascular endothelia other proliferative processes are not manifest, particularly not with reference to the uriniferous epithelia. Inflammatory reaction is likewise not seen. There is neither an interstitial round-cell infiltration nor the presence of fibrous interstitial tissue. The changes found in the kidney tissue proper all appear to be exclusively the result of pressure and pressure atrophy.

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